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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/939,230	08/24/2001	Alan David Wickenden	018512-006610US	5203

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EXAMINER	
JONES, DWAYNE C	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 03/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/939,230	WICKENDEN ET AL.	
	Examiner	Art Unit	
	Dwayne C. Jones	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *the amendment and declaration of 22DEC05*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45-57,60-63,65-69 and 83* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45-57,60-63,65-69 and 83* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Claims 45-57, 60-63, 65-69, and 83 are pending.

2. Claims 45-57, 60-63, 65-69, and 83 are rejected.

3. Claims 1-44, 58, 59, 64, and 70-82 are cancelled.

Response to Arguments

4. Applicants' arguments and declaration filed December 22, 2005 have been reviewed and considered. The following arguments were presented by applicants. First, applicants argues as well as the declaration of Dr. Krafte sets forth a large number of structurally diverse KCNQ channel openers with scope of amended claim 45. Second, the arguments and the declaration also submit that there are a number of assays known in the art to identify KCNQ channel openers. Third, applicants argue that the presence of only one working example should never be the sole reason for rejecting claims as being broader than the alleged enabling disclosure.

5. First, applicants argues as well as the declaration of Dr. Krafte sets forth a large number of structurally diverse KCNQ channel openers with scope of amended claim 45. The claims teach of amide containing compounds with the variables of X, Ar^1, and Ar^2. In addition, these variables can represent countless compounds with the limitless possibilities that are conceived by the claimed formula and variables of the amended claims. In particular, the variable of Ar^1 can be represented by seven (7) different aryl compounds whereas the variable of Ar^2 can be represented by any and all compounds

that are only described as being aryl or heteroaryl. Considering the unpredictability of synthetic chemistry, particularly with those compounds having multiple heteroaryl ring systems, the level of the skilled artisan, and the fact that applicants provide no clear directed, guidance, and working examples, other than those compounds of Figure 7, regarding how to obtain the compounds claimed and employed herein, it is apparent that applicants fail to provide information allowing the skilled artisan to ascertain these compounds without undue experimentation.

6. Moreover, the instantly claimed subject matter does not fully support the breadth of the instant claims, especially with the functional phrase embracing all compounds that are broadly claimed as being able "to increase ion flow through KCNQ potassium channels" or even that the compounds of claims 45-57 and 60-63 because each of the variables, namely X, Ar^1, and Ar^2, can represent countless compounds with the limitless possibilities that are conceived by the claimed formula and variables of the amended claims. For example, the variable of Ar^2 can be represented by any and all compounds that are only described as being aryl or heteroaryl. And so, these claims can be embraced by any aryl group, any and all heteroaryl moieties under the sun, which can allegedly treat anxiety. In addition, applicants arguments are not commensurate in scope with inter alia independent claim 45 and dependent claims 46-57 and 60-63 because one skilled in the art of neuropharmacology is not provided with enablement, such as with sufficient guidance and predictability in the art and working examples for every compound that falls under the umbrella of the functional phrase embracing all

compounds that are broadly claimed as being able "to increase ion flow through KCNQ potassium channel."

7. Second, the arguments and the declaration also submit that there are a number of assays known in the art to identify KCNQ channel openers. Applicants' are enabled identifying the compounds of Figure 7 but not for each and every compound that is are functionally described as being able "to increase ion flow through KCNQ potassium channels" and to treat the condition of anxiety especially when the variable of Ar^2 can be represented by any and all compounds that are only described as being aryl or heteroaryl.

8. Third, applicants argue that the presence of only one working example should never be the sole reason for rejecting claims as being broader than the alleged enabling disclosure. However, the fact remains that the instantly claimed subject matter does not fully support the breadth of the instant claims, especially with the functional phrase embracing all compounds that are broadly claimed as being able "to increase ion flow through KCNQ potassium channels" or even that the compounds of claims 58 or 70 because each of the variables in these claims can be any aryl group, any and all heteroaryl moieties under the sun, which can allegedly treat anxiety. Moreover, this allegation is not found persuasive because the elucidation of a biochemical mechanism with already known aryl and heteroaryl carbamoyl compounds are known in the art to treat the very same condition of anxiety. Accordingly, the presence of a working example is just one factor to be considered when enablement is at an issue, as it is presently in this application. In addition, applicants further argue that a working in vivo

example is provided in the treatment of anxiety. This one example only provides one skilled in the art with a showing of how a rat reacts with a hot plate.

Claim Rejections - 35 USC § 112

9. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

10. The rejection of claims 45-57 and 60-63 are under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the compounds of aryl amide containing compounds of Figure 7 for the treatment of anxiety, does not reasonably provide enablement ford other compounds that are functionally described as being known as a compound that increases ion flow through KCNQ potassium channels in a cell is maintained and repeated for both the above stated and reasons of record. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are

weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention:

The instant invention is directed to treating anxiety. The method comprises administering a compound that is functionally described as increasing ion flow through KCNQ potassium channels in a cell.

(2) The state of the prior art

The compounds of the inventions are functionally described as increasing ion flow through KCNQ potassium channels in a cell. However, the prior art does not teach that these functionally described as increasing ion flow through KCNQ potassium channels in a cell possess these types of properties, see Leppert et al. and Gaster et al.

(3) The relative skill of those in the art

The relative skill of those in the art of pharmaceuticals is very high.

(4) The predictability or unpredictability of the art

The unpredictability of the pharmaceutical art is very high. In fact, the courts have made a distinction between mechanical elements functioning the same in different circumstances, yielding predictable results, but chemical and biological compounds often react unpredictably under different circumstances. Nationwide Chem. Corp. v.

Wright, 458 F. Supp. 828, 839, 192 USPQ 95, 105(M.D. Fla. 1976); Aff'd 584 F.2d 714, 200 USPQ 257 (5th Cir. 1978); In re Fischer, 427 F.2d 833, 839, 166 USPQ 10, 24 (CCPA 1970). Thus, the physiological activity of a chemical or biological compound is considered to be an unpredictable art. For example, in Ex Parte Sudilovsky, the Court held that Appellant's invention directed to a method for preventing or treating a disease known as tardive dyskinesia using an angiotensin converting enzyme inhibitor involved unpredictable art because it concerned the pharmaceutical activity of the compound. 21 USPQ2d 1702, 1704-5 (BDAI 1991); In re Fisher, 427 F.2d 1557, 1562, 29 USPQ, 22 (holding that the physiological activity of compositions of adrenocorticotropic hormones was unpredictable art; In re Wright, 999 F.2d 1557, 1562, 29 USPQ d, 1570, 1513-14 (Fed. Cir. 1993) (holding that the physiological activity of RNA viruses was unpredictable art); Ex Parte Hitzeman, 9 USPQ2d 1821, 1823 (BDAI 1987); Ex Parte Singh, 17 USPQ2d 1714, 1715, 1716 (BPAI 1990). Likewise, the physiological or pharmaceutical activity of a compound that is functionally described as increasing ion flow through KCNQ potassium channels in a cell, including carbamoyl-containing compounds that have aryl as well as heteroaryl moieties prior to filing of the instant invention was an unpredictable art.

(5) The breadth of the claims

The instant claims are very broad. For instance, claim 45 is directed to the plethora of compounds that are embraced by the functional description increasing ion flow through KCNQ potassium channels in a cell. The breadth of claims was a factor in

Amgen v. Chugai Pharm. Co., 927 F.2d 1200, 18 USPQ2d (Fed. Cir.),cert. Denied, 502 U.S. 856 (1991). In the Amgen case, the patent claims were directed to DNA sequences that encoded amino acid sequences. Because a very small change in the amino acid sequence of a protein can result in a very large change in the structure-function activity of a protein and because the laws of protein folding are in such a primitive state, predicting protein structure (and hence, activity) while knowing only the sequence of the protein is akin to predicting the weather for a date in the future.

(6) The amount of direction or guidance presented

The amount of guidance or direction needed to enable the invention is inversely related to the degree of predictability in the art. In re Fisher, 839, 166 USPQ 24. Thus, although a single embodiment may provide broad enablement in cases involving predictable factors, such as mechanical or electrical elements, in cases involving unpredictable factors, such as most chemical reactions and physiological activity, more teaching or guidance is required. In re Fischer, 427 F.2d 839, 166 USPQ 24; Ex Parte Hitzeman, 9 USPQ 2d 1823. For example, the Federal Circuit determined that, given the unpredictability of the physiological activity of RNA viruses, a specification requires more than a general description and a single embodiment to provide an enabling disclosure for a method of protecting an organism against RNA viruses. In re Wright, 999 F.2d 1562-63, 27 USPQ2d 1575. In the instant case, given the unpredictability of the physiological or pharmaceutical activity of compounds that are embraced by the functional description increasing ion flow through KCNQ potassium channels in a cell to

be effective in treating anxiety is insufficient for enablement. The specification provides no guidance, in the way of enablement for compounds that are embraced by the functional description of increasing ion flow through KCNQ potassium channels in a cell along with including carbamoyl-containing compounds that have aryl as well as heteroaryl moieties other than the compounds of aryl amide containing compounds of Figure 7 for the treatment of anxiety. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also In re Wright, 999 F.2d 1557, 27 USPQ2d 1510 (Fed. Cir. 1993); In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). This is because it is not obvious from the disclosure of one species, what other species will work. In re Dreshfield, 110 F.2d 235, 45 USPQ 36 (CCPA 1940), gives this general rule: "It is well settled that in cases involving chemicals and chemical compounds, which differ radically in their properties it must appear in an applicant's specification either by the enumeration of a sufficient number of the members of a group or by other appropriate language, that the chemicals or chemical combinations included in the claims are capable of accomplishing the desired result." The article "Broader than the Disclosure in Chemical Cases," 31 J.P.O.S. 5, by Samuel S. Levin covers this subject in detail. A disclosure should contain representative examples, which provide reasonable assurance to one skilled in the art that the compounds that fall within the scope of a claim will possess the alleged activity. See In re Riat et al. (CCPA 1964) 327 F2d 685, 140 USPQ 471; In re Barr et al. (CCPA 1971) 444 F 2d 349, 151 USPQ 724.

(7) The presence or absence of working examples

As stated above, the specification discloses compounds that are embraced by the functional description increasing ion flow through KCNQ potassium channels in a cell that have are used to treat anxiety. However, the instant specification only has enablement for the compounds of aryl amide containing compounds of Figure 7 for the treatment of anxiety.

(8) The quantity of experimentation necessary

The quantity of experimentation needed to be performed by one skilled in the art is yet another factor involved in determining whether "undue experimentation" is required to make and use the instant invention. "'The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.'" In re Wands, 858 F.2d 737, 8 USPQ2d 1404 (citing In re Angstadt, 537 F.2d 489, 502-04, 190 USPQ 214, 218 (CCPA 1976)). For these reasons, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to determine all of the compounds that are embraced by the functional description increasing ion flow through KCNQ potassium channels in a cell that would be enabled in this specification.

11. Claims 45-57 and 60-63 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject

matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

12. *Regents of the University of California v. Eli Lilly & Co.., 119 F.3d 1559, 1568 (Fed. Cir. 1997), cert. denied, 523 U.S. 1089, 118 S.Ct. 1548 (1980),* holds that an adequate written description requires a precise definition, such as by structure, formula, chemical name, or physical properties, "not a mere wish or plan for obtaining the claimed chemical invention." *Eli Lilly, 119 F.3d at 1566.* The Federal Circuit has adopted the standard set forth in the Patent and Trademark Office ("PTO") Guidelines for *Examination of Patent Applications Under the 35 U.S.C. 112, 1 "Written Description" Requirement ("Guidelines"), 66 Fed. Reg. 1099 (Jan. 5, 2001)*, which state that the written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics, "including, inter alia, "functional characteristics when coupled with a known or disclosed correlation between function and structure...." *Enzo Biochem, Inc. v. Gen-Probe., 296 F.3d, 316, 1324-25 (Fed. Cir. 2002)* (quoting Guidelines, 66 Fed. Reg. At 1106 (emphasis added)). Moreover, although *Eli Lilly* and *Enzo* were decided within the factual context of DNA sequences, this does not preclude extending the reasoning of those cases to chemical structures in general. *Univ. of Rochester v. G.D. Searle & Co., 249 F. Supp.2d 216, 225 (W.D.N.Y 2003).*

13. There is insufficient descriptive support for the terms "aryl" and "heteroaryl". In addition, the instant specification does not describe what is meant by the terms "aryl"

and "heteroaryl" other than the compounds of aryl amide containing compounds of Figure 7. Structural identifying characteristics of the terms "aryl" and "heteroaryl" are not disclosed except for those the compounds of aryl amide containing compounds of Figure 7. There is no evidence that there is any per se structure/function relationship between the terms "aryl" and "heteroaryl" other than those disclosed, namely the compounds of aryl amide containing compounds of Figure 7. The instant specification does not provide an adequate written description for the terms "aryl" and "heteroaryl". Accordingly, these claims fail to comply with the written description requirement.

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 45-57 and 60-63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons support this rejection. The terms "aryl" and "heteroaryl" are indefinite. What is the size of the "aryl" or the "heteroaryl" ring or ring system? What is the number and nature of the heteroatoms in the "heteroaryl" ring or ring system? Can the rings be fused, connected or linked or even spiro-conncected to another ring or ring system? Can the ring or rings by bridged? Are all the rings in the ring or ring system aryl or is there a degree of unsaturation?, In re Wiggins, 179, 179 USPQ 421, 423. The instant specification provides no clear definition for the terms "aryl" and "heteroaryl", please refer to pages 19 and 20 of the specification.

Claim Rejections - 35 USC § 103

16. The rejection of claims 45-48, 54-59, 61-65, 70, 71, and 72 under 35 U.S.C. 103(a) as being unpatentable over Gaster et al. of U.S. Patent No. 6,235,758 is withdrawn in response to the amendment of December 22, 2005.

Obviousness-type Double Patenting

17. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

18. The rejection of claims 45-57 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 46-67 of McNaughton-Smith et al. of U.S. Patent No. 6,593,349 is withdrawn in response to the amendment of December 22, 2005.

19. The rejection of claims 45-82 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 46-67 of U.S. Patent No. 6,235,758 is withdrawn in response to the amendment of December 22, 2005.

20. The rejection of claims 45-57, 60-63, 65-69, and 83 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 22 of U.S. Patent No. 6,495,550 is maintained and repeated. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant invention and U.S. Patent No. 6,495,550 teach of treating anxiety with the administration of aryl and heteroaryl carbamoyl-containing compounds that modulate a voltage dependent potassium channel.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. C. Jones whose telephone number is (571) 272-0578. The examiner can normally be reached on Mondays, Tuesdays, Thursday, and Fridays from 8:30 am to 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, may be reached at (571) 272-0951. The official fax No. for correspondence is (703) 872-9306.

Also, please note that U.S. patents and U.S. patent application publications are no longer supplied with Office actions. Accordingly, the cited U.S. patents and patent application publications are available for download via the Office's PAIR, see http://pair-direct.uspto.gov. As an alternate source, all U.S. patents and patent application publications are available on the USPTO web site (www.uspto.gov), from the Office of Public Records and from commercial sources.

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DWAYNE JONES
PRIMARY EXAMINER

Tech. Ctr. 1614
March 15, 2006